December 7, 1949.

Dr. P. R. Edwards,
Communicable Disease Center,
Enteric Bacteriology Laboratory,
Chamblee, Georgia.

Dear Dr. Edwards:

Thank you very much for the diagnosis of the S. coli strains sent you. These strains had not been exposed to deleterious agents, and were simply found in the stock which we had maintained without repurification since receipt from Borman in Connecticut. It was a relief to learn that we had good grounds (since both are S. coli 1) to reject the disturbing idea that the culture was mixed because of our own technical incompetence. The two cultures have certainly diverged in an interesting way. I shall try to find out whether they are ultimately derived from E. coli 134; as I mentioned, Borman's label read " 548 "m and he had implied that it was ultimately gotten from you.

I would be very interested to consult with you concerning the possibility of phage isolations for diagnostic purposes. Within limits, phages might be of great value in epidemiological work. My own experience, and what I have been able to learn from the literature suggests, however, that there will be only the most general parallelism between phage typings and serotypes. It probably would not be possible, in general, to obtain monospecific phages whose host range would be exactly congruent with the distribution of a given somatic antigen or complex. However, within a given serotype, phages might be useful in untangling epidemiological traces. The sort of work that Lilleengen has been doing with typhimurium should be extended.

I would like to take this opportunity to bring up another suggestion, which I may, perhaps, have stated imperfectly to you before. The hasty, and extensive (rather than intensive) survey that I made on the nutrition of Salmonella strongly suggested that, within serotypes, there may be a number of distinctive nutritional sub-types. This is especially true of S. pullorum and gallinarum, which are officially "lumped" because of their

common somatic antigen, but which are nutritionally and pathologically distinctive. The few gallinarum strains which I have studied, or heard tell of, invariably require no more than thiamin as a nutritional supplement, whereas pullorum strains generally require a number of amino acids, usually including cystine and leucine. I believe that it is the low cystine content of most ordinary media which is responsible for the slow growth that is usually mentioned as a "cultural" characteristic of these strains. This correlation should be studied more thoroughly, and if supported with a variety of isolates originally characterized by their disease-producing characteristics, should be the most precise method for laboratory diagnosis of these non-motile Salmonellas.

But I also feel that possibly less distinctive subtypes of other serotypes should also be characterizable by their nutritional requirements. I believe that it is unfortunate that Hohn and Harrmann went so far in their claims for the "ammonstark" characteristic, especially at a time when the interpretation of bacterial growth on synthetic media was less well understood. Their generalizations concerning the far-reaching biological significance of auxo-autotrophy are patently fallacious, but I think that theybhave induced a reaction which obscures a proper consideration of the potential usefulness of nutritional studies.

As somewhat of a minor corrolary of my plaintive remarks, I would like to point out something of the significamce of the "citrate" test as applied, for example, to the S. coli I sent you. An organism will fail to grow on a synthetic medium with citrate as sole carbon source under either of the following circumstances: 1) if it is unable to utilize citrate as a carbon or energy source, or2) if although potaatially able to utilize citrate, it is unable to grow due to a requirement for an additional growth factor(s). In the present instance, the S. coli Lac+ is unable to grow owing to a requirement for histidine; the typical E. coli is citrate-negative for reason (1). Even if it were felt that a more thorough nutritional examination was too ambitious a program, I feel that the differential value of the "citrate" test could be greatly amplified, and put on a more rational basis, if it were accompanied by a parallel test on a synthetic glucose medium. Glucose-negative organisms are sufficiently rare in this group that inability to grow on a glucose-synthetic medium would imply a nutritional requirement (2), while ability to grow on glucose-synthetic but not on citrate would imply the incompetence to utilize citrate (1).

I hope that we may have an opportunity to discuss these matters in more detail sometime- perhaps at the next national SAB meeting.

Sincerely yours,

Joshua Lederberg
Assistant Professor of Genetics